



## Department of Public Health, Office of Medical Cannabidiol

### Laboratory Testing Requirements & Acceptance Criteria

#### Table of Contents

<b>1.0 Introduction and Purpose .....</b>	<b>2</b>
<b>2.0 Definitions .....</b>	<b>3</b>
<b>3.0 Sampling Plan .....</b>	<b>5</b>
<b>4.0 Contaminant Analysis and Acceptance Criteria .....</b>	<b>7</b>
<b>5.0 Test Failure Process .....</b>	<b>11</b>
<b>6.0 Cannabinoid Content Testing .....</b>	<b>12</b>
<b>7.0 Stability Testing .....</b>	<b>13</b>

## **1.0 Introduction and Purpose**

### **1.1 – Introduction**

The vision of the Office of Medical Cannabidiol (OMC) at the Iowa Department of Public Health is to have a high-quality, effective, and compliant medical cannabidiol program for Iowa residents with serious medical conditions. Once implemented, the program will ensure access to medical cannabidiol products to patients with serious medical conditions at five dispensaries across the state.

OMC will work to balance a patient's need for access to low-cost treatments with the requirement to ensure the safety and efficacy of the products. Paramount to patient safety and care is making sure that each medical cannabidiol product sold to a patient is tested for harmful contaminants and that product labels accurately reflect the content and potency of the medical cannabidiol being dispensed.

### **1.2 – Purpose**

The purpose of this document is to provide licensed Iowa medical cannabidiol manufacturers and laboratories with the required and recommended best practices for the collection and analysis of medical cannabidiol and other finished medical cannabidiol products. The governing statute of the Office of Medical Cannabidiol is Iowa Code chapter 124E and the associated administrative rules are found in 641 Iowa Administrative Code chapter 154.

*This document is subject to revision based on evolving best practices, updated scientific information or standards and guidelines, changes in laws or regulations, and other information relevant to the contents of the protocol.*

## 2.0 Definitions

**Acceptance criteria:** The specified limits placed on characteristics of an item or method that are used to determine data quality with the exception of microbiological testing. When an acceptance criteria for microbiological quality is prescribed, the maximum acceptable counts are as follows:

Colony-Forming Unit (CFU)	Maximum Acceptable Count
$10^1$	20
$10^2$	200
$10^3$	2000 and so forth

*Reference: USP 1111 Microbiological Examination of Nonsterile Products: Acceptance Criteria for Pharmaceutical Preparations and Substances for Pharmaceutical Use.*

**Action level:** The threshold value that provides the criterion for determining whether a sample passes or fails a test performed pursuant to 641 IAC 154.

**Analyte:** A chemical, compound, element, bacteria, yeast, fungus, or toxin to be identified or measured.

**Certificate of Analysis:** A document released by the laboratory to the manufacturer and department, which contains the concentrations of cannabinoid analytes and other measures approved by the department, as well whether a sample passed or failed in accordance with 641 IAC 154.

**Cannabinoid Content Testing:** The testing of final medical cannabidiol products for cannabinoid analytes, including: THC, THCa, CBD, CBDa, CBG, and CBN.

**Department:** The Iowa Department of Public Health.

**Laboratory:** The State Hygienic Laboratory at the University of Iowa or other independent medical cannabidiol testing facility accredited to Standard ISO/IEC 17025 by an ISO-approved accrediting body, with a controlled substance registration certificate from the Drug Enforcement Administration of the U.S. Department of Justice and a certificate of registration from the Iowa board of pharmacy, and approved by the department to examine, analyze, or test samples of medical cannabidiol or any substance used in the manufacture of medical cannabidiol.

## 2.0 Definitions

**Lot:** A specific quantity of medical cannabidiol that is uniform and intended to meet specifications for identity, strength, purity, and composition, and that is manufactured, packaged, and labeled during a specified time period according to a single manufacturing, packaging, and labeling record. For the purposes of this document, there are process lots and packaged lots.

**Lot number:** A unique numeric or alphanumeric identifier assigned to a lot by a manufacturer when medical cannabidiol is produced. The lot number shall contain the manufacturer's number and a sequence to allow for inventory, traceability, and identification of the plant batches used in the production of a lot of medical cannabidiol.

**Medical Cannabidiol:** Any pharmaceutical grade cannabinoid found in the plant *Cannabis sativa* L. or *Cannabis indica* or any other preparation thereof that has a tetrahydrocannabinol level of no more than 3 percent and that is delivered in a form recommended by the medical cannabidiol board, approved by the board of medicine, and adopted by rule.

**Process lot:** Any amount of cannabinoid concentrate or extract that is uniform, produced from one or more batches, and used for testing for identity, strength, purity, and composition prior to being formulated into a product.

**Packaged lot:** A finished lot of medical cannabidiol that has been packaged but has not been transported or sold to a dispensary.

**Stability Testing:** The process by which a manufacturer determines the expiration date or shelf life of a given form and dose of medical cannabidiol.

## 3.0 Sampling Plan

### 3.1 – Sampling Plan Overview

Development of sampling strategies is a requirement of licensed manufacturers described in 641 IAC 154.26(2). This document is designed to outline sampling procedures recommended to manufacturers by the Office of Medical Cannabidiol. Samples submitted for process lot testing should be representative of the entire process lot, and samples of packaged lots should be representative of products for sale to patients.

### 3.2 – Process Lot Sampling

For testing at the process lot stage, extracts should be thoroughly mixed before sampling to ensure homogenization of the sample. Samples of medical cannabidiol process lots should be collected following distillation but before processing into products. Manufacturers must contact the laboratory in advance to schedule a transfer of samples in accordance with 641 IAC 154.22.

Contaminants tested at the process lot stage include: *Pesticides, Residual Solvents and Processing Chemicals, Metals, and Total Yeast and Mold*. Action levels and criteria for contaminants can be found in **Table 4**.

The required samples for a given process lot will be taken by mass (g), and will follow the strategy as outlined below in **Table 1**.

Table 1 – Process Lot Sampling			
Process Lot Weight		Sample Increments Required (1.0g ± 0.2g)	
Pounds	Kilograms	# of Samples	Reserve Samples
0-0.50	1-0.23	2	1
0.50-1.50	0.24-0.68	4	1
1.51-3.00	0.69-1.36	6	1
3.10-6.0	1.40-2.72	8	1
6.10-10.00	2.77-4.54	10	1
10+	4.58+	15	2

For reserve samples, two samples will be taken for every 15 primary samples.

### 3.0 Sampling Plan

For a 4.50+ Kilogram process lot, sampling will follow the strategy as outlined in **Table 2**.

*\* Mass is sampled in grams for all analytes. The number indicates the mass of process necessary per sample.*

The State Hygienic Laboratory will provide weighed and designated containers for analytes. Microbiological samples will be taken from container #1, and metals, pesticides and solvents will be drawn from container #2.

Table 2 – Process Lot Sampling (4.5 kg+)						
	Analytes Tested					1 & 2 Total
	Container #1	Container #2				
Sample #	Micro	Metals	Pesticides	Solvents	Transfer Loss	
1	0.5	0.5	0.1	0.1	0.1	1.3
2	0.5	0.5	0.1	0.1	0.1	1.3
3	0.5	0.5	0.1	0.1	0.1	1.3
4	0.5	0.5	0.1	0.1	0.1	1.3
5	0.5	0.5	0.1	0.1	0.1	1.3
6	0.5	0.5	0.1	0.1	0.1	1.3
7	0.5	0.5	0.1	0.1	0.1	1.3
8	0.5	0.5	0.1	0.1	0.1	1.3
9	0.5	0.5	0.1	0.1	0.1	1.3
10	0.5	0.5	0.1	0.1	0.1	1.3
11	0.5	0.5	0.1	0.1	0.1	1.3
12	0.5	0.5	0.1	0.1	0.1	1.3
13	0.5	0.5	0.1	0.1	0.1	1.3
14	0.5	0.5	0.1	0.1	0.1	1.3
15	0.5	0.5	0.1	0.1	0.1	1.3
Reserve #1	0.5	0.5	0.1	0.1	0.1	1.3
Reserve #2	0.5	0.5	0.1	0.1	0.1	1.3
Matrix Spike (QC)	0	0.5	0.1	0.1	0.1	0.8
Total Mass for Testing	8.5	9	1.8	1.8	1.8	22.9
Containers by Test	17	18				35

## 3.0 Sampling Plan

### 3.3 – Packaged Lot Sampling

For testing at the packaged lot stage, manufacturers shall submit samples of packaged products prior to the products being transferred or delivered to dispensaries. Samples sent for testing should include all excipients and other products that are in final products, and shall be representative of final packaged products. Samples being tested shall not be more dilute than product available for patients. Manufacturers must contact the laboratory in advance to schedule a transfer of samples in accordance with 641 IAC 154.22.

Testing at the packaged lot stage will include: *Microbiological Impurities* and *Content Testing for Cannabinoids*. If the introduction or use of *solvents or processing chemicals* after process lot testing is discovered by the department or disclosed by the manufacturer, testing for residual solvents and processing chemicals shall occur at the packaged lot stage as well. Packaged product cannabinoid content will be determined for THC, THCa, CBD, CBDa, CBG, and CBN. Tests for microbiological impurities will be done to ensure that contamination was not introduced after processing. Cannabinoid content testing will be done on packaged lots to ensure correct and compliant dosing of products. Action levels and criteria for contaminants can be found in **Table 4**.

The required samples for a given packaged lot will follow the strategy as outlined below in **Table 3**.

Table 3 – Packaged Lot Sampling		
Units for Sale	Sample Units	Reserve Samples
2-15	2	1
16-50	3	1
51-150	5	1
151-500	8	1
501-3,200	13	1
3,201-35,000	20	1

For each packaged lot, a manufacturer shall retain a uniquely labeled reserve sample, consisting of twice as much as is necessary to perform all the required tests. The sample shall represent each packaged lot of medical cannabidiol, and shall be stored for two years under conditions consistent with product labeling and in the same or similar container-closure system in which the product is marketed and sold (641 IAC 154.26(5)).

## 4.0 Contaminant Analyses and Acceptance Criteria

Approved laboratories and licensed manufacturers should refer to **Table 4** to guidelines for product testing and acceptance criteria.

Table 4 - Contaminant Analysis & Acceptance Criteria			
Analyte	Action Level	Comment	Guideline
<b>Metals</b>		Metals testing is required for every process lot	FDA Q3D, elemental impurities guidance
Arsenic	1.5 ppm		
Cadmium	0.3 ppm		
Lead	1.0 ppm		
Mercury	0.5 ppm		
Analyte	Action Level	Comment	Guideline
<b>Microbiological Impurities</b>	See Table 5	Only one microbial test (Total combined yeasts molds) performed for process lots; this test and other microbial testing are performed for product lots  For microbial analytes and acceptance criteria, see <b>Table 5</b>	American Herbal Pharmacopeia (USP 1111), State of Iowa Hygienic Laboratory
Analyte	Action Level	Comment	Guideline
<b>Pesticides</b>	See Table 6-	Pesticide Testing is required for every process lot  For pesticide analytes and action levels, see <b>Table 6</b>	APHL "Guidance for State Medical Cannabis Testing Programs" (2016)
Analyte	Action Level	Comment	Guideline
<b>Solvents</b>		Solvent testing is required for every process lot	Based on disclosed use by manufacturer
Ethanol	5000 ppm		

*\*For all contaminants, a test shall be reported as having failed if the analyte concentration is above the action level approved by the department and listed in this document.*

## 4.0 Contaminant Analyses and Acceptance Criteria

Table 5 – Microbiological Impurities & Acceptance Criteria				
Microbiological Test	Testing Stage (Lot)	Consumable products	Inhalable products	Non-consumable Products (Topical, Suppositories)
Total aerobic microbial count	Product	1x10 <sup>3</sup> CFU/g Max acceptable count: 2000	1x10 <sup>2</sup> CFU/g Max acceptable count: 200	1x10 <sup>3</sup> CFU/g Max acceptable count: 2000
Total combined yeasts molds count	Process, Product	1x10 <sup>2</sup> CFU/g Max acceptable count: 200	1x10 <sup>1</sup> CFU/g Max acceptable count: 20	1x10 <sup>2</sup> CFU/g Max acceptable count: 200
<i>Aspergillus</i> ( <i>A.fumigatus</i> , <i>A. flavus</i> , <i>A. niger</i> , <i>A. terreus</i> )*	Product		No detection in 1 g	
Shiga-Toxin Producing <i>E.coli</i>	Product	No detection in 1 g	No detection in 1 g	
<i>Salmonella</i>	Product	No detection in 1 g	No detection in 1 g	

\*Results for this test will only be reported when mold is found on the Total Combined Yeasts Molds Count.

## 4.0 Contaminant Analyses and Acceptance Criteria

Table 6 – Pesticide Analytes and Action Levels		
Analyte	Chemical Abstract Services (CAS) Registry Number	Action Level (ppm)
Acetamiprid	135410-20-7	0.2
Aldicarb	116-06-3	0.4
Azoxystrobin	131860-33-8	0.2
Bifenazate	149877-41-8	0.2
Boscalid	188425-85-6	0.4
Carbaryl	63-25-2	0.5
Carbofuran	1563-66-2	0.2
Chlorantraniliprole	500008-45-7	0.2
Chlorpyrifos	2921-88-2	0.6
Cypermethrin	52315-07-8	18
Diazinon	333-41-5	2.6
Dichlorvos	62-73-7	0.1
Ethoprophos	13194-48-4	0.4
Etofenprox	80844-07-1	0.4
Fipronil	120068-37-3	1
Flonicamid	158062-67-0	1
Imidacloprid	138261-41-3	0.4
Metalaxyl	57837-19-1	0.2
Methiocarb	2032-65-7	0.4
Methomyl	16752-77-5	0.4
Methyl parathion	298-00-0	8.5
Myclobutanil	88671-89-0	0.3
Oxamyl	23135-22-0	1
Permethrin I	52465-53-1	1.1
Pyridaben	96489-71-3	0.2
Spiroxamine I	118134-30-8	2
Tebuconazole	80443-41-0	0.4
Thiacloprid	111988-49-9	0.2
Thiamethoxam	153719-23-4	0.2

## **5.0 Test Failure Process**

### **5.1 – Process Lot Testing Failure**

If a failure occurs for any of the listed contaminants at the process lot stage, pursuant to 641 IAC 156.26(3)c, a manufacturer shall refrain from packaging or selling medical cannabidiol from a process lot that fails to meet established standards, specifications, and any other relevant quality control criteria. Medical cannabidiol from a process lot that fails contaminant testing at the process lot stage may be remixed and retested. The manufacturer will retain this option in perpetuity at the process lot stage assuming remediation is possible.

### **5.2 – Packaged Lot Testing Failure**

If a packaged lot sample submitted for testing for microbiological impurities fails testing at the packaged lot stage, the manufacturer has discretion to determine if the packaged lot can be remediated and resubmitted for testing. The same protocol will be followed for medical cannabidiol from a packaged lot that fails quality assurance testing based on cannabinoid content.

## **6.0 Cannabinoid Content Testing**

At the packaged lot stage, a laboratory shall test and report measurement for the following cannabinoid analytes: THC, THCa, CBD, CBDa, CBG, and CBN.

A laboratory shall report that the primary sample passed cannabinoid content testing for THC if the detected concentration of THC does not exceed 3% by weight in milligrams per milliliter (mg/ml) for liquids, milligrams per gram (mg/g) for solids and if the detected concentration of THC does not vary from the manufacturer's labeled concentration by more than 15 percent by weight in mg/ml for liquids and mg/g for solids. The test shall be reported as having failed potency testing if the THC concentration is greater than 3% for either liquids or solids, or the THC concentration varies from labeled concentration by more than 15%.

A laboratory shall report that the primary sample passed cannabinoid content testing for CBD if the detected concentration of CBD does not vary from the manufacturer's labeled concentration by more than 15% by weight in mg/ml for liquids and mg/g for solids, and shall report as having failed if variance is more than 15% from the labeled concentration.

## 7.0 – Stability Testing

As a part of a quality control program, manufacturers shall develop procedures for performing stability testing of each product type that is manufactured. Stability testing shall be done in the same container-closure system in which the product is sold.

Licensed manufacturers should refer to **Table 7** guidelines for sample size and testing intervals for stability testing.

Table 7 – Stability Testing									
Product	Sample size tested at each interval	Sample container	Storage Conditions	Intervals (months)					
Capsule	3 capsules	White Plastic Bottle	Room Temp.	0	3	6	9	12	18
Suppository	3 suppositories	Blister Pack	Room Temp.	0	3	6	9	12	18
Tincture	0.5 mL	Amber Glass Bottle	Room Temp.	0	3	6	9	12	18
Lotion	1.0 mL	White Plastic Bottle	Room Temp.	0	3	6	9	12	18

If product-expiration-date studies have not been completed before a manufacturer begins delivering products to dispensaries, the manufacturer shall assign a tentative product expiration date, not to exceed one year, based on any available stability information (641 IAC 154.26(4)).